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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,541	03/01/2002	Benjamin R. Halpern	ABIOS.022A	2245
7590	12/12/2007		EXAMINER	
Leonard D. Bowersox, Esquire KILYK & BOWERSOX, P.L.L.C. 3603-E Chain Bridge Road Fairfax, VA 22030			BORIN, MICHAEL L	
			ART UNIT	PAPER NUMBER
			1631	
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			12/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/087,541	HALPERN, BENJAMIN R.	
	<b>Examiner</b> Michael Borin	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 18 September 2007.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-15, 17 and 19-27 is/are pending in the application.
  - 4a) Of the above claim(s) 1-7 and 11 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 8-10, 12-27 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.
 

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
    - a) All    b) Some \* c) None of:
      1. Certified copies of the priority documents have been received.
      2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
      3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/18/2007 has been entered.

### ***Status of Claims***

Claims 1-15, 17,19-27 are pending. Claim 8 is amended. Claims 1-7, 11 remain withdrawn from further consideration as being drawn to a non-elected groups.

### ***Claim Rejections - 35 USC § 103.***

Claims 8-10,12-27 are rejected under 35 U.S.C. 103(a) as unpatentable over Eriksson et al in view of Arnold et al. and further in view of Wilkins (J. Mol. Biol. 1999, 289,645-657).

The instant claims are drawn to method for comparing a modified query peptide to a plurality of database peptides. "Modified" means polypeptide modified by any post-translational modification, such as phosphorylation, oxidation, substitution, etc, which alters mass of the query polypeptide. The claimed method comprises the steps of: (a)

identifying a fragmentation spectrum comprising a plurality of query mass values for query peptide; (b) dividing spectral range of the modified peptide into intervals, c) evaluating peptide fragments in each interval, and comparing fragments in each of said plurality of intervals with known fragments, scoring the fragments and identifying best matching fragments. A spectral range is the range from zero to the unmodified query peptide's mass. The claims are now amended to add a step specifying that scores of the mass ratio comparison for each range of a query peptide fragment and known peptides is summed up before the identifying step.

Eriksson et al (US Patent 6,466,010) teaches method for assessing significance of protein identification. The method comprises steps of generating mass data for fragments of a query polypeptide (e.g., claim 1) wherein the polypeptide may have post-translational modifications (see col. 9, lines 42-44; claim 28) and compared to protein database, wherein the database comprises information on polypeptides which exhibit modifications. The query polypeptide is cleaved into parts by a method that produces constituent parts in a predictable way (claim 42), and comparison can be constrained within a chosen mass range (claims 45, 47).

With regard to scoring, Eriksson teaches that mass comparison is scored with the score scores denoting a degree of similarity between data. A comparison is performed until sufficient quantity of scores is selected. See col. 8 and col. 12, first and second paragraph.

With regard to b-ions and y-ions (new claims 20-22, 24,25) In the process of collision-induced dissociation, a peptide bond at a random position is broken, and each

molecule is fragmented into two *complementary* ions, typically an N-terminal ion called *b-ion* and a C-terminal ion called *y-ion*. Therefore, b- and y-ions are formed in the method of Eriksson.

Eriksson et al does not teach apportioning the spectral range into plurality of divisions.

Arnold et al teaches that matching of results of mass spectrometry with databases can be substantially improved by dividing spectral range into intervals. The reference teaches that dividing spectral range into intervals allows fine-tuning of correlation analysis and yields correlation indices that are more sensitive to spectral differences. See abstract, and p. 635. For example mass range from 3.5 to 10 kDa was divided into 13 intervals of 500 Da each before running comparative analysis. See p. 631, left column, bottom.

It would be *prima facie* obvious to one skilled in the art at the time the invention was made to be motivated to divide spectral range into plurality of divisions while using method of Eriksson et al because such subdivision into intervals was shown by Arnold to be beneficial for more precise detection and determination of spectral differences which is a desirable feature for spectral analysis of modified peptides in the method of Eriksson et al .

With regard to repeating identifying for each fragment and then summing up the scores obtained from the intervals, as now addressed in the claims, Eriksson et al obviously would not teach such summing up because the method compares scores

obtained for the entire molecule. Col. 8, lines 23-25. However, as one would be motivated to divide spectral range into plurality of divisions while using method of Eriksson et al, as addressed above, and because Eriksson et al compares scores obtained for the entire molecule, one would be then motivated to sum up the scores obtained for each of the intervals.

With regard to the limitation of excluding or adjusting modified mass ratios, the reference of Eriksson, although it does not teach excluding or adjusting modifications before comparative analysis, it addresses the issue of accounting for post-translational modifications. see col. 9, lines 39-61.

Wilkins teaches software FindMod which can identify post-translational modifications in residues of unknown peptides. Identifying such modifications thus allows to subtract their mass and compare thus corrected mass values of peptide with database data. Thus, for example, Wilkins describe a peptide of mass 1631 which did not match any database entry; however, after identifying potential modification and subtracting its value, the sequence of peptide was identified.

Combining known prior art elements is not sufficient to render the claimed invention obvious if the results would not have been predictable to one of ordinary skill in the art. KSR v. Teleflex, No. 04-1350, 550 U.S. \_\_\_\_ (2007). As all the claimed elements were known in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable

results to one of ordinary skill in the art at the time of the invention.

Therefore, It would be *prima facie* obvious to one skilled in the art at the time the invention was made to be motivated to apply approach of Wilkins in the scoring method of Eriksson to be able to match mass information of a query peptide and known database information because identification and removal of modified information allows more precise comparison with database information and thus enables identification of sequence of query protein which is the objective of mass-spectrum analysis.

Response to arguments

Applicant states that the combination of the references does not teach the claimed invention. In particular, applicant Eriksson does not teach distributing entire range into intervals. Indeed, as stated in the rejection, apportioning the spectral range into plurality of divisions is not taught by Eriksson , and is taught by Arnold. With regard to the latter reference applicant argues that the matching of the intervals is not based on "postulated" fragment modifications. Examiner agrees- the reference of Arnold is used to demonstrate the motivation for subdivision of full range into intervals which would be beneficial for more precise detection and determination of spectral differences. The reference of Arnold is not used to address post-translational modifications. In addition, per instant claims, dividing into intervals does not depend on presence/absence of post-translational modifications; only after the spectral range is split into intervals, the presence of such modifications is postulated. In turn, Wilkens reference teaches how to deal with post-translational modifications. As all the claimed elements were known

in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention.

***Double Patenting***

The provisional rejection of claim 8-10,12-27 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/241751 is maintained for the reasons of record.

Applicant has indicated previously that filing Terminal Disclaimer will be considered upon identification of allowable subject matter in the instant application. In turn, Examiner will revise the issue of double patenting upon identification of allowable subject matter in the instant application.

***Conclusion.***

No claims are allowed.

This is an RCE of applicant's earlier Application No.10/087541. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL**

even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
Michael Borin, Ph.D.  
Primary Examiner  
Art Unit 1631

mlb